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Predictive value of neutrophil-to-lymphocyte ratio for adverse outcomes in hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease

A retrospective study

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Abstract

Chronic obstructive pulmonary disease (COPD) stands as one of the leading causes of mortality worldwide. Acute exacerbations of COPD (AECOPD) lead to rapid respiratory function decline and worsened disease status. Despite recent studies, the ability of the neutrophil-to-lymphocyte ratio (NLR) to predict outcomes in patients with COPD remains controversial. We investigated the predictive value of NLR for adverse outcomes in hospitalized patients with AECOPD. A retrospective study was conducted at the Department of Pulmonary Medicine, Cho Ray Hospital (Vietnam) from November 2019 to November 2021. The study extracted data from patients diagnosed with AECOPD at discharge and met the inclusion criteria. NLR is calculated by dividing the number of neutrophils by the number of lymphocytes in the peripheral blood test. Adverse outcomes are defined as invasive mechanical ventilation, admission to intensive care unit, or in-hospital mortality. Multivariable regression analysis was conducted to identify variables predicting adverse outcomes. The cutoff, sensitivity, specificity, area under the curve, and receiver operating characteristic of NLR were determined for predicting adverse outcomes. Two hundred eighty-seven patients with AECOPD were included in the final analysis, with a mean age of 70.9, and males comprising 92.7%. The rate of adverse outcomes was 15.7%. Multivariable logistic regression identified reduced consciousness at admission (adjusted odds ratio = 0.08, 95% confidence interval [CI]: 0.02–0.38, $P = .001$) and high NLR (adjusted odds ratio = 1.17, 95% CI: 1.10–1.24, $P < .001$) as predictors of adverse outcomes. The receiver operating characteristic of NLR's predictive value yielded an area under the curve of 0.877 (95% CI: 0.83–0.93). An NLR cutoff of 11.0 predicted adverse outcomes with a sensitivity of 80.0%, specificity of 77.7%, and an odds ratio of 13.9 (95% CI: 6.3–30.7), $P < .001$. NLR is a simple, routine, and cost-effective tool for predicting adverse outcomes in hospitalized patients with AECOPD. Future studies should evaluate the kinetics of NLR in predicting treatment response in patients with AECOPD.

Abbreviations: AECOPD = acute exacerbations of COPD, AOR = adjusted odds ratio, CI = confidence interval, COPD = chronic obstructive pulmonary disease, GCS = Glasgow coma scale, GOLD = global initiative for chronic obstructive lung disease, ICD = international classification of diseases, NLR = neutrophil-to-lymphocyte ratio, SD = standard deviation, WBC = white blood cells.

Keywords: adverse outcomes, chronic obstructive pulmonary disease, exacerbation, mortality, neutrophil-to-lymphocyte ratio

1. Introduction

Chronic obstructive pulmonary disease (COPD) stands as one of the leading causes of mortality worldwide, posing an increasing economic burden.[1–3] With the rising rates of smoking in developing countries and population aging in developed nations, COPD is predicted to increase in the future, affecting over 175 million people and becoming the fourth leading cause of death by 2040.[4,5] Acute exacerbations of COPD (AECOPD)

Informed consent was obtained from the patient.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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are defined as acute deterioration of respiratory symptoms requiring additional treatment, leading to rapid respiratory function decline, diminished quality of life, and worsened disease status.[6,7]

Neutrophils are the most common type of white blood cells (WBC) and participate in multiple inflammatory and immune processes through phagocytosis and cytokine release.[8] Lymphocytes play a crucial role as coordinators of the inflammatory and immune processes in various physiological mechanisms.[9,10] The neutrophil-to-lymphocyte ratio (NLR) is calculated by dividing the number of neutrophils by the number of lymphocytes in the peripheral blood test, reflecting an increase in neutrophils and a secondary decrease in lymphocyte count during the inflammatory response.[11,12] The NLR is considered a biological marker reflecting the inflammatory condition and is increasingly recognized in various disorders such as pneumonia, malignant, coronary artery disease, or hematological disorders.[11–14]

Günay et al[15] were the first to utilize NLR to assess the severity of the inflammatory response in patients with COPD. Subsequent studies suggested that NLR is an independent predictor of AECOPD,[16,17] mortality,[16,18–20] and hospitalization[17] in patients with COPD. However, the predictive value of NLR in patients with AECOPD remains unclear. Lee et al[21] demonstrated that NLR was not associated with AECOPD. Sorensen indicated that NLR was not a prognostic factor for mortality in patients with COPD treated with systemic corticosteroids.[22] Studies have investigated the role of NLR in severe AECOPD requiring hospitalization.[12,18,20,23–26] However, the majority of these studies predominantly focus on the predictive role of NLR in mortality, with limited information regarding its ability to predict intensive care unit (ICU) admission or the need for invasive mechanical ventilation. Additionally, most of these studies have been conducted in developed countries. Therefore, the role of NLR in hospitalized severe AECOPD in developing countries, particularly in those with a high burden of tuberculosis, warrants further investigation.

The investigation for a simple, convenient, and rapid tool to evaluate the severity of inflammatory response and predict clinical outcomes in AECOPD is essential, especially in developing countries. From the results reported by recent studies, it remains controversial whether NLR can predict clinical outcomes in hospitalized patients with AECOPD. Therefore, we conducted this study to investigate the predictive value of NLR for adverse outcomes in hospitalized patients with AECOPD.

2. Materials and methods

A retrospective study was conducted at the Department of Pulmonary Medicine, Cho Ray Hospital (Vietnam) from November 2019 to November 2021. The study extracted data from patients diagnosed with AECOPD at discharge and met the inclusion criteria.

2.1. Inclusion criteria

We recruited patients aged 18 and above and extracted medical records from the hospital database containing diagnoses at discharge with the international classification of diseases codes J44.0 (chronic obstructive pulmonary disease with acute lower respiratory infection) or J44.1 (chronic obstructive pulmonary disease with acute exacerbation, unspecified) over 2 years (November 2019 to November 2021). Our department diagnoses patients with AECOPD based on the global initiative for chronic obstructive lung disease 2021 criteria, which define AECOPD as acute exacerbations of respiratory symptoms necessitating additional treatment, resulting in rapid decline in respiratory function, decreased quality of life, and deterioration of disease status.[27]

2.2. Exclusion criteria

We excluded medical records that included: patients transferred to other hospitals, patients who refused treatment, patients admitted with initial diagnoses other than AECOPD, and medical records lacking complete blood count tests.

2.3. Sample size

We used the following formula to calculate the sample size based on a proportion[28]:

$$n = \frac{Z^2{}_{1-\frac{\alpha}{2}} \times p(1-p)}{d^2}$$

$Z_{1-\alpha/2}$ is the corresponding coefficient for a 95% confidence interval (CI), where $\alpha = 5\%$; p is the proportion of adverse outcomes; $p = 15.89\%$ based on a study by Fang et al[12]; d is the standard error. We chose $d = 5\%$. Therefore, our study would require a minimum of 207 participants.

2.4. Definition of variables

Comorbidities such as hypertension, coronary artery disease, gastroesophageal reflux disease, history of pulmonary tuberculosis, diabetes, Cushing syndrome, chronic kidney disease, cancer, heart failure, atrial fibrillation, cirrhosis were recorded based on medical history and final diagnoses at discharge. Reduced consciousness was defined as the absence of head trauma history and the Glasgow Coma Scale (GCS) score <15 points, according to Quintana et al.[29] This assessment was performed by emergency department physicians at the time of patient admission and recorded in the medical records. Hypotension at admission was defined as systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or vasopressor usage. The values of WBC, neutrophils, lymphocytes, eosinophils, and platelets were recorded in the peripheral blood count test was performed immediately after admission. Arterial blood gas values were also recorded at admission, including pH and $PaCO_2$. NLR is calculated by dividing the number of neutrophils by the number of lymphocytes in the peripheral blood test.

Our department applies invasive mechanical ventilation criteria for patients with AECOPD as follows: failure of noninvasive ventilation, cardiopulmonary arrest, altered mental status, agitation, risk of aspiration, inability to expectoration, hemodynamic instability despite fluid resuscitation and vasopressor therapy, severe ventricular or atrial dysrhythmias, threatened hypoxemia.

Adverse outcomes are defined as invasive mechanical ventilation, admission to ICU, or in-hospital mortality.[12]

2.5. Statistical analysis

The statistical analysis was performed using STATA version 15.1 (StataCorp, College Station, TX). Continuous variables were presented as mean ± standard deviation or median (interquartile range) for nonnormally distributed data. Categorical variables were presented as frequency counts and percentages. Fisher exact test, or χ^2 test, was used to compare the frequency of binary variables. The Mann–Whitney U test was used to compare continuous variables. Compare the NLR between the group with and without adverse outcomes: check the normal distribution using the Kolmogorov–Smirnov test. If the data follows a normal distribution, perform the Student t test; if not, conduct the Mann–Whitney U test. Utilize the receiver operating characteristic curve to determine sensitivity, specificity, and the area under the curve (AUC) to evaluate NLR in predicting adverse outcomes. Variables were included in the multivariate analysis if their P value in the univariate analysis was <.2.[30–32] This approach ensures that all relevant and potentially

predictive variables are examined. A P value <.05 was considered statistically significant.

2.6. Study protocol

The study protocol is shown in Figure 1.

2.7. Medical ethics

The Ethical Review Committee at the University of Medicine and Pharmacy at Ho Chi Minh City provided approval for the study (No. 556/HĐĐĐ-ĐHYD, November 11, 2021).

3. Results

From November 2019 to November 2021, a total of 343 medical records were diagnosed with AECOPD at discharge at the Department of Pulmonary Medicine, Cho Ray Hospital. Among these, 19 cases were initially diagnosed with conditions other than AECOPD upon admission, 12 cases were transferred to other hospitals, and 25 cases refused treatment. Therefore, 287 patients with AECOPD were included in the final analysis (Fig. 1).

3.1. Patient characteristics

The study population had a mean age of 70.9 and males comprised the majority (92.7%). The most common comorbidity was hypertension (48.4%), while a history of previous pulmonary tuberculosis was recorded in approximately one-fifth of cases. The percentages of patients with reduced consciousness and hypotension at admission were 8.4% and 2.4%, respectively. There were 16 deaths with a mortality rate of 5.6%. Forty-two patients required invasive mechanical ventilation and ICU admission, among whom 13 died (31%). The rate of adverse outcomes was 15.7%. Additional information regarding the baseline characteristics of the study population can be found in Table 1.

3.2. Factors associated with adverse outcomes

Univariate analysis of clinical factors related to adverse outcomes, including age, body mass index, hypertension, coronary artery disease, heart failure, diabetes, chronic kidney disease, reduced consciousness, and hypotension at admission, revealed that in the group of AECOPD with adverse outcomes, the prevalence of reduced consciousness and hypotension at admission was significantly higher, with P values of < .001 (Table 2).

Univariate analysis of laboratory factors revealed that in the group of patients with AECOPD with adverse outcomes, the WBC, neutrophil counts, NLR, blood urea nitrogen, and arterial $PaCO_2$ level were significantly higher compared to the group without adverse outcomes (all P values < .05). Conversely, in the group of patients with AECOPD with adverse outcomes, the number of lymphocytes, eosinophils, and arterial pH were significantly lower compared to the remaining group (all P values < .05) (Table 3).

Variables with a P value <.2 were included in a multivariable logistic regression model, with a significance threshold set at $P < .05$. These variables included coronary artery disease, reduced consciousness at admission, hypotension, NLR, eosinophils, platelet counts, blood urea nitrogen, creatinine, arterial pH, and arterial $PaCO_2$. Multivariable logistic regression analysis revealed that reduced consciousness at admission (adjusted odds ratio = 0.08, 95% CI: 0.02–0.38, $P = .001$) and high NLR (adjusted odds ratio = 1.17, 95% CI: 1.10–1.24, $P < .001$) were associated with increased odds of adverse outcomes (Table 4).

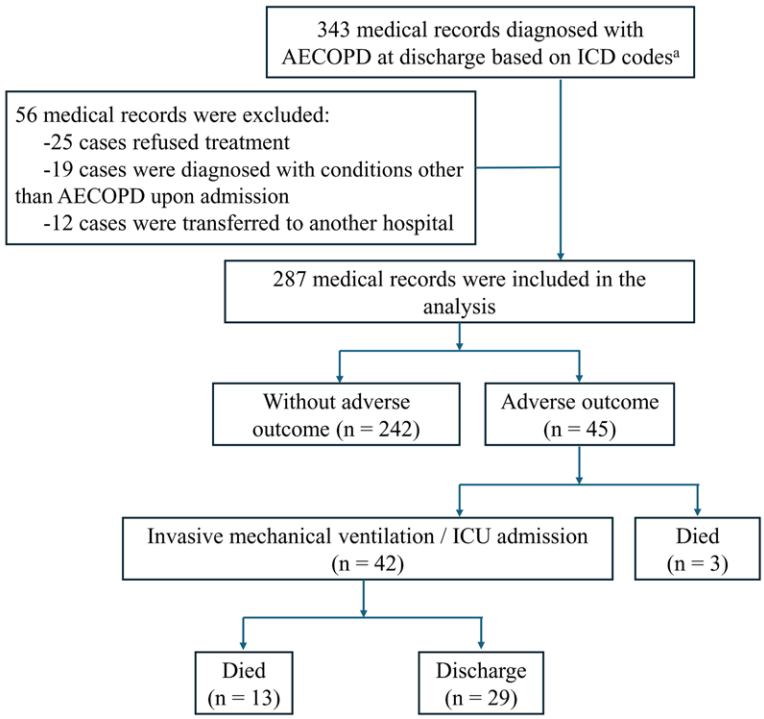
343 medical records diagnosed with AECOPD at discharge based on ICD codes[a]
56 medical records were excluded:
-25 cases refused treatment
-19 cases were diagnosed with conditions other than AECOPD upon admission
-12 cases were transferred to another hospital
287 medical records were included in the analysis
Without adverse outcome (n = 242)
Adverse outcome (n = 45)
Invasive mechanical ventilation / ICU admission (n = 42)
Died (n = 3)
Died (n = 13)
Discharge (n = 29)

Figure 1. Study protocol. [a]J44.0 (chronic obstructive pulmonary disease with acute lower respiratory infection), J44.1 (chronic obstructive pulmonary disease with acute exacerbation, unspecified). AECOPD = acute exacerbations of chronic obstructive pulmonary disease, ICD = international classification of diseases, ICU = intensive care unit.

3.3. The relationship between the NLR and adverse outcomes in hospitalized patients with AECOPD

The NLR value was significantly higher in the adverse outcome group compared to the nonadverse outcome group (20.4 [11.5–29.9] and 6.0 [3.5–10.3], $P < .001$, Mann–Whitney U test), with an odds ratio of 1.18 (95% CI: 1.12–1.23) (Fig. 2). Using the receiver operating characteristic curve to evaluate the predictive value of NLR for adverse outcomes in hospitalized patients with AECOPD, our study yielded an AUC of 0.877 (95% CI: 0.83–0.93). We identified an NLR cutoff of 11.0 for predicting the risk of adverse outcomes, including invasive mechanical ventilation, admission to the ICU, and in-hospital mortality, with a sensitivity of 80.0%, specificity of 77.7%, and an odds ratio of 13.9 (95% CI: 6.3–30.7), $P < .001$. NLR has an AUC of 0.798 (95% CI: 0.70–0.90) for predicting mortality in AECOPD patients. An NLR cutoff of 11.5 for predicting the risk of mortality, with a sensitivity of 81.2% and a specificity of 72.7%.

Table 1

Baseline and clinical characteristics of the study population (n = 287).

Variables	n (%)	Mean ± SD
Age (yr)		70.9 ± 10.1
<60	44 (15.3)	
60–80	196 (68.3)	
>80	47 (16.4)	
Male	266 (92.7)	
Female	21 (7.3)	
Body mass index (kg/m^2)		21.3 ± 3.7
Hypertension	139 (48.4)	
Coronary artery disease	70 (24.4)	
Gastroesophageal reflux disease	56 (19.5)	
History of pulmonary tuberculosis	55 (19.2)	
Diabetes	45 (16.0)	
Cushing syndrome	41 (14.3)	
Chronic kidney disease	14 (4.9)	
Cancer	13 (4.5)	
Heart failure	11 (3.8)	
Atrial fibrillation	8 (2.9)	
Cirrhosis	7 (2.4)	
Reduce consciousness at admission	24 (8.4)	
Hypotension at admission	7 (2.4)	
Invasive mechanical ventilation	42 (14.6)	
Intensive care unit admission	42 (14.6)	
Death	16 (5.6)	
Adverse outcome*	45 (15.7)	

SD = standard deviation.

*Including invasive mechanical ventilation, intensive care unit admission, and death.

4. Discussion

The main finding of this 2-year retrospective study on patients hospitalized with AECOPD revealed an adverse outcome rate of 15.7%. Significant predictors of adverse outcomes identified through multivariable logistic regression analysis included reduced consciousness at admission and NLR.

Most cases of AECOPD are mild and suitable for outpatient treatment. However, approximately 3% to 16% of AECOPD cases require hospitalization or admission to the ICU.[33,34] AECOPD significantly contributes to the rapid decline in respiratory function (forced expiratory volume in the first second), increases mortality rates, and severely affects the quality of life. Our study indicates that the overall mortality rate for hospitalized patients with AECOPD is 5.6%, consistent with other studies reporting mortality rates ranging from 5.3% to 10.4%.[12,35,36] However, once AECOPD patients are admitted to the ICU or require invasive ventilation, the mortality rate increases significantly, ranging from 14% to 57%.[36–41] Our study found that 31% of patients admitted to the ICU or requiring invasive ventilation died. Notably, the long-term prognosis for these AECOPD patients is also poor, with 1-year and 5-year mortality rates of 40% and 70%, respectively.[38,42] Therefore, there is a need for a simple and convenient tool to predict adverse outcomes in hospitalized patients with AECOPD at primary healthcare levels, enabling timely identification and close monitoring of high-risk cases.

Currently, numerous models evaluate prognostic factors for mortality and unfavorable outcomes in AECOPD, offering prediction tools with relatively high accuracy by combining clinical and laboratory characteristics. However, the assessment and identification of these risk factors remain inconsistent across reports due to the complex pathogenesis of COPD and its overlap with other comorbidities. Investigated risk factors include high acute physiology and chronic health evaluation II scores, low GCS scores, advanced age, prolonged hospital stay, cardiopulmonary arrest, metabolic acidosis, hypoalbuminemia, multiple organ failure, and comorbidity risk index.[35,43–45] However, some risk factors indicate that the patient is already in a severe condition (low GCS scores, metabolic acidosis, multiple organ failure, etc) and

Table 2

Clinical factors associated with adverse outcomes (n = 287).

Variables	Without adverse outcome (n = 242)	With adverse outcome (n = 45)	*P*
Age (yr)	70.9 ± 10.2	70.8 ± 9.4	.95*
Male	226 (93.4)	40 (88.9)	.29†
Body mass index (kg/m^2)	21.2 ± 3.7	21.8 ± 3.3	.29*
Hypertension	118 (48.8)	21 (46.7)	.80†
Coronary artery disease	64 (26.4)	6 (13.3)	.06†
Gastroesophageal reflux disease	46 (19.0)	10 (22.2)	.62†
History of pulmonary tuberculosis	44 (18.1)	11 (24.4)	.33†
Heart failure	8 (3.3)	3 (6.7)	.28†
Diabetes	38 (15.7)	7 (15.6)	.98†
Cushing syndrome	35 (14.5)	6 (13.3)	.84†
Chronic kidney disease	13 (5.4)	1 (2.2)	.37†
Cancer	12 (4.9)	1 (2.2)	.42†
Atrial fibrillation	6 (2.5)	2 (4.4)	.46†
Cirrhosis	5 (2.1)	2 (4.4)	.34†
Reduce consciousness at admission	6 (2.5)	18 (40.0)	**<.001**†
Hypotension at admission	2 (0.8)	5 (11.1)	**<.001**†

The P value < .05 is highlighted in bold.

*Student t test.

†Fisher exact test.

Table 3

Laboratory factors associated with adverse outcomes (n = 287).

Variables	Total	Without adverse outcome (n = 242)	With adverse outcome (n = 45)	*P*
WBC (K/μL)	10.7 (8.0–13.9)	10.1 (7.7–13.0)	14.2 (12.0–17.6)	**<.001***
Neutrophil (K/μL)	8.0 (5.7–11.2)	7.4 (5.3–9.9)	12.5 (10.2–15.7)	**<.001***
Lymphocyte (K/μL)	1.1 (0.7–1.6)	1.2 (0.8–1.7)	0.6 (0.4–1.0)	**<.001***
NLR	7.1 (3.9–13.7)	6.0 (3.5–10.3)	20.4 (11.5–29.9)	**<.001***
Eosinophil (K/μL)	0.1 (0.02–0.3)	0.1 (0.03–0.4)	0.02 (0–0.08)	**<.001***
Platelet counts (G/L)	252 (201–316)	256 (204–330)	230 (200–280)	.09*
BUN (mg/dL)	17 (13–25)	16 (12–22)	25 (18–33)	**<.001***
Creatinine (mg/dL)	0.9 (0.7–1.1)	0.8 (0.7–1.0)	0.9 (0.7–1.3)	.08*
Arterial pH	7.40 ± 0.12	7.42 (7.35–7.49)	7.35 (7.25–7.45)	**.002***
Arterial $PaCO_2$ (mm Hg)	51.7 ± 22.8	41.3 (34.6–61.3)	54.3 (38.3–80.3)	**.03***

The data are presented as mean ± standard deviation or median (interquartile range). The *P* value < .05 is highlighted in bold.

BUN = blood urea nitrogen, NLR = neutrophil-to-lymphocyte ratio, WBC = white blood cells.

*Mann–Whitney *U* test.

Table 4

Univariate and multivariable analysis for predicting adverse outcomes.

	Model 1*			Model 2†	
Variable	OR	*P*	AOR	95% CI	*P*
Coronary artery disease	2.33	.06	2.19	0.66–7.30	.20
Reduce consciousness at admission	0.04	<.001	0.08	0.02–0.38	**.001**
Hypotension at admission	15.00	.002	3.54	0.31–40.4	.31
NLR	1.18	<.001	1.17	1.10–1.24	**<.001**
Eosinophil count	0.03	.003	0.42	0.05–3.90	.45
Platelet count	1.00	.11	0.99	0.99–1.00	.58
Creatinine	1.75	.01	1.12	0.48–2.59	.80
BUN	1.05	<.001	1.03	0.98–1.08	.21
Arterial pH	0.01	.001	0.49	0.001–315	.83
Arterial $PaCO_2$	1.02	.007	1.02	0.99–1.05	.26

The *P* value < .05 is highlighted in bold.

AOR = adjusted odds ratio, BUN = blood urea nitrogen, CI = confidence interval, NLR = neutrophil-to-lymphocyte ratio, OR = odds ratio.

*Model 1: univariable logistic regression analysis.

†Model 2: multivariable logistic regression analysis.

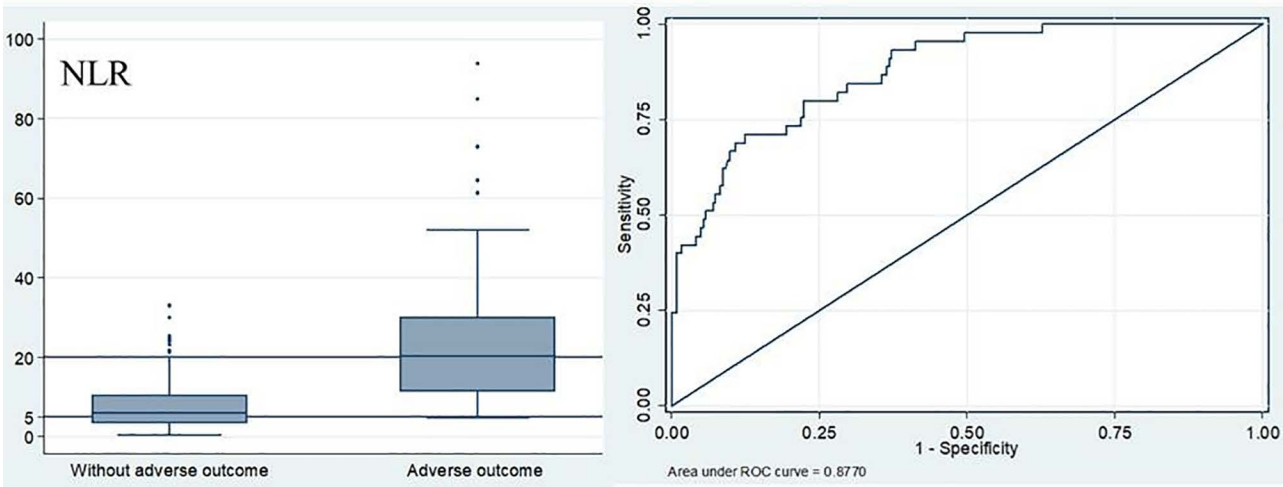

Figure 2. Predictive value of neutrophil-to-lymphocyte ratio and adverse outcomes in hospitalized patients with chronic obstructive pulmonary disease. NLR = neutrophil-to-lymphocyte ratio, ROC = receiver operating characteristic curve.

requires immediate intervention, thus limiting their utility in predicting adverse outcomes in hospitalized patients with AECOPD.

In recent years, there have been multiple studies on the role of NLR in predicting AECOPD, mortality, and the need for invasive ventilation in patients with COPD. However, most studies differ in their sample selection criteria, outcome definitions, and study designs, leading to a wide range of reported NLR cutoff values. A 2018 review encompassing 20 studies on NLR in patients with COPD revealed cutoff values ranging from 2.56 to 16 for predicting AECOPD, hospitalization, in-hospital mortality, or infections during exacerbations.[11] Despite its widespread use, achieving consensus on the optimal NLR value in patients with COPD remains challenging. The NLR comprises 2 components: blood neutrophil and

Table 5

The value of the neutrophil-to-lymphocyte ratio in predicting mortality, invasive ventilation, and adverse outcomes across studies.

Author (yr)	Population	Outcome	NLR cutoff	Sensitivity	Specificity	AUC	95% CI
Our study (Vietnam, 2022)	287 hospitalized AECOPD patients	Adverse outcomes*	≥11.0	80.0%	77.7%	0.877	0.83–0.93
		In-hospital mortality	≥11.5	81.2%	72.7%	0.798	0.70–0.90
Lu et al (China, 2021)[12]	282 severe AECOPD with frequent exacerbations	Adverse outcomes*	≥10.2	62.1%	92.0%	0.833	0.77–0.89
Yao et al (China, 2017)[18]	303 hospitalized AECOPD patients	In-hospital mortality	≥6.2	81.1%	69.2%	0.803	
Teng et al (China, 2018)[26]	906 hospitalized AECOPD patients	Invasive ventilation	≥10.3	54.3%	84.8%	0.732	0.66–0.81
		28-d mortality	≥8.1	60.5%	74.8%	0.737	0.66–0.81
Karauda (Poland, 2021)[24]	275 hospitalized AECOPD patients	In-hospital mortality	≥13.2	100%	92.6%	0.96	0.93–0.99
Rahimirad (Iran, 2017)[20]	315 hospitalized AECOPD patients	In-hospital mortality	≥4	87.0%	40.0%	0.717	0.62–0.81
Aksoy et al (Turkey, 2018)[23]	10592 AECOPD patients	In-hospital mortality	≥8.0	78.0%	60.0%	0.78	0.69–0.87
Saltürk et al (Turkey, 2015)[25]	647 AECOPD patients and admitted to the ICU	In-hospital mortality	≥16				

AECOPD = acute exacerbation of chronic obstructive pulmonary disease, AUC = area under the curve, CI = confidence interval, ICU = intensive care unit, NLR = neutrophil-to-lymphocyte ratio.
*Including invasive mechanical ventilation, intensive care unit admission, or in-hospital mortality.

lymphocyte counts. Consequently, changes in either component affect the NLR. First, NLR values are significantly higher in patients with AECOPD compared to those with stable COPD (12.4 ± 10.6 vs 2.4 ± 0.7, respectively).[21] Second, the NLR cutoff value for predicting mortality is higher than that for predicting AECOPD (ranging from 3.3 to 16 vs 2.8 to 4.69).[46] Third, patients with a frequent exacerbation phenotype show higher NLR values compared to those without frequent exacerbations (5.93 [3.40–9.28] vs 4.41 [2.74–6.80]).[12] Fourth, factors unrelated to COPD, such as age and infections, also influence NLR. Infections can increase neutrophil counts and decrease lymphocyte counts.[11,12] while advanced age has been shown to reduce lymphocyte numbers.[47] Finally, the use of systemic corticosteroids and prior antibiotic treatment can affect NLR, rendering it less meaningful for predicting mortality.[22] Table 5 includes the value of NLR in predicting mortality, invasive ventilation, and adverse outcomes across various studies. Two similar studies[12,26] that used NLR to predict the need for invasive mechanical ventilation reported NLR values approximately equivalent to our study, around 11.0.

Table 5 demonstrates that our study's cutoff value for NLR in predicting adverse outcomes is similar to that of Lu et al,[12] and the prediction of invasive mechanical ventilation is comparable to Teng et al.[26] However, there is a significant variation in the cutoff values for NLR in predicting mortality in AECOPD, ranging from 4 to 16 across different studies.[18,20,23–26] Our study identifies a cutoff NLR value of 11.5 for predicting mortality, which is higher than those reported by Yao et al,[18] Teng et al,[26] Rahimirad et al,[20] and Aksoy et al,[23] but lower than the values reported by Saltürk et al[25] and Karauda et al.[24] In the study by Yao et al,[18] the population had a younger average age (61 compared to 70.9 in our study). This age difference may account for the lower NLR, as lymphocyte count tends to decrease with age.[47] Additionally, their study reported a lower $PaCO_2$ level (46.5 compared to 51.7 mm Hg in our study), which may indirectly indicate a higher severity of AECOPD in our study, contributing to the increased cutoff value for NLR. The difference in the cutoff value of NLR for predicting mortality may also originate from the definition of the variable. Teng et al[26] defined mortality as death within 28 days, whereas most other studies defined it as in-hospital mortality. Finally, the study design plays a crucial role in the variation of NLR cutoff values for predicting mortality. Aksoy et al[23] included all AECOPD patients, including those treated on an outpatient basis, resulting in a lower NLR cutoff. Conversely, Saltürk et al[25] focused solely on AECOPD patients admitted to the ICU, leading to the highest NLR cutoff value. Consequently, the wide variation in NLR cutoff values for predicting mortality can be attributed to several objective factors.

Despite numerous studies demonstrating the value of NLR in predicting mortality in hospitalized AECOPD patients, current research is limited by its retrospective nature. Consequently, no studies have yet evaluated interventions aimed at reducing NLR to improve patient outcomes in AECOPD. Teng et al[26] reported a decrease in NLR after patient improvement (6.89 ± 6.82 at admission compared to 4.19 ± 5.11 after treatment, $P = .000$). Aksoy et al[23] also suggested that AECOPD patients with neutrophilic cell predominance (peripheral blood eosinophil <2% and NLR ≥4) might benefit from initiating antibiotic therapy. However, whether such interventions enhance outcomes remains to be determined by larger, future studies.

Our study has several limitations. First, being a retrospective study, complete information on previous exacerbations within the past year or respiratory function test results may not have been documented, thereby limiting our ability to assess the severity of COPD. Second, the study did not analyze the effects of medications in treatment such as antibiotics, bronchodilators, and corticosteroids. This could overlook patients who have not received appropriate treatment and lead to disease progression. Finally, the study did not assess the dynamics of NLR in response to AECOPD treatment.

5. Conclusion

NLR is a simple, routine, and cost-effective tool for predicting adverse outcomes in hospitalized patients with AECOPD. Future studies should evaluate the kinetics of NLR in predicting treatment response in patients with AECOPD.

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